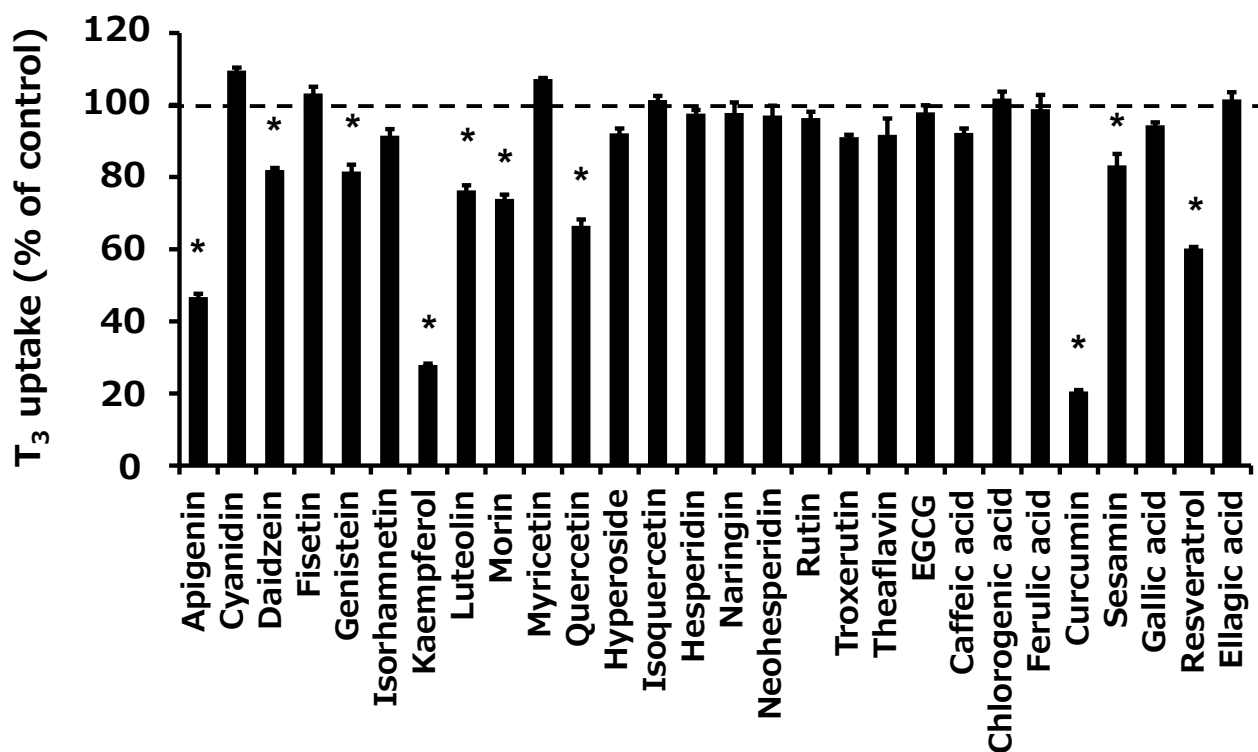


Supplementary Materials Data



Scheme 1. Screening of the effect of food ingredients on OATP4C1-mediated transport under the presence of AA. Cells were incubated with 1 μ M T_3 with or without food ingredients for 10 min at 37 °C under the presence of 10 μ M AA. The concentrations of the compounds were 100 μ M except for theaflavin (50 μ M). The amount of OATP4C1-mediated uptake was calculated by subtracting the nonspecific uptake of T_3 by mock cells from the total cellular uptake by the OATP4C1-expressing cells. Data are shown as mean \pm standard error (S.E.) (n = 3). * p < 0.05, significantly different from control by one-way analysis of variance followed by Tukey's test.

Scheme 1. Inhibition parameters of food ingredients for OATP4C1 and other drug transporters in the liver and kidney.

Inhibition (IC ₅₀ or K _i values (μM)) or elevation (EC ₅₀ values (μM)) parameters							
Compounds	OATP4C1	OATP1B1	OATP1B3	OATP2B1	OAT1	OAT3	P-gp
Apigenin	Yes (54%, 100 μM)	0.6 ± 0.2 ^{1*} 53.4 ± 2.1 ¹ Yes ²	16.7 ± 1.6 ^{1*}	13.9 ± 1.6 ³ 20.8 ± 8.0 ³	0.212 ± 0.010 ⁴	0.410 ± 0.157 ⁴	-
Cyanidin	Yes (24%, 100 μM)	-	-	Yes ⁵ 22.3 ± 2.2 ⁶	-	-	-
Daidzein	Yes (40%, 100 μM)	-	-	Yes ⁵ 20.7 ± 4.3 ⁶	-	-	-
Fisetin	No	Yes ²	-	-	Yes ⁷	-	-
Genistein	Yes (42%, 100 μM)	14.9 ± 3.76 ²	-	8.6 ± 1.8 ⁶ Yes ⁵ 4.6 ± 2.5 ⁶	-	-	Yes ⁸
Isorhamnetin	Yes (18%, 100 μM)	3.12 ⁹ 46.12 ± 5.25 ¹⁰	3.10 ⁹	0.82 ⁹	-	-	-
Kaempferol	25.1 ± 1.6*	16.0 ± 1.9 ^{1*} 32.4 ± 2.2 ¹ 33.05 ¹¹ 3.28 ± 1.08 ¹⁰	24.4 ± 1.8 ^{1*}	15.1 ± 7.8 ^{3*} 20.7 ± 1.8 ³ Yes ⁵	-	-	Yes ¹²
Luteolin	Yes (52%, 100 μM)	22.03 ¹¹ 0.85 ¹³ Yes ²	-	Yes ⁵ 0.42 ¹³	0.47 ⁷ 5.17 ¹⁴	4.20 ¹⁴	-
Morin	Yes (57%, 100 μM)	Yes ²	-	-	< 0.3 ⁷ 0.5 ¹⁵	-	Yes ¹⁶
Myricetin	No	Yes ²	-	-	Yes ⁷	-	-
Quercetin	Yes (50%, 100 μM)	8.8 ± 0.8 ^{1*} 9.1 ± 1.0 ¹ 15.9 ± 1.4 ¹⁷ 1.55 ⁹ 3.28 ± 1.08 ¹⁰ 1.82 ¹⁸	7.8 ± 1.7 ^{1*} 3.22 ⁹	8.7 ± 0.1 ^{3*} 14.1 ± 1.3 ³ Yes ⁵ 0.34 ⁹ 7.5 ± 1.2 ¹⁹	Yes ⁷	-	Yes ²⁰
Hyperoside	No	-	-	29.4 ± 1.5 ¹⁹	-	-	-
Hesperidin	No	-	-	Yes ⁵ 72.3 ± 1.4 ¹⁹ >300 ²¹ 8.3 ± 1.2 ²² 37.0 ²³	-	-	-
Naringin	No	Yes (<50%, 250 μM) ¹	197.5 ± 1.1 ¹	36.4 ± 8 ²¹ 6.9 ± 1.4 ²²	-	-	Yes ²⁴
Rutin	No	Yes (<50%, 150 μM) ¹ Elevation (81.1%, 50 μM) ²	111.5 ± 1.1 ¹	60.7 ± 1.2 ¹⁹	-	-	Yes ²⁰
Theaflavin	No	-	-	8.2 ± 1.7 ^{5*}	-	-	Yes ²⁰
EGCG	No	14.1 ± 1.4 ² 7.8 ± 0.9 ²⁵	Elevation (EC ₅₀ =10.5 ± 1.6) ²⁵ 8.4 ± 0.6 ²⁵	101 ± 9 ²⁵ Yes ²⁶	334 ± 58 ^{27*}	162 ± 29 ^{27*}	Yes ²⁰
Caffeic acid	No	-	-	-	5.22 ²⁸ 16.6 ± 3.7 ²⁹	30.8 ²⁸ 5.4 ± 1.3 ²⁹	Yes ³⁰
Ferulic acid	No	-	-	-	9.01 ²⁸	7.35 ± 3.73 ³¹	Yes ³²
Curcumin	23.5 ± 0.5*	3.81 ³³	33.7 ³³	Yes ⁵	-	-	Yes ³⁴
Gallic acid	No	-	1.60 ± 0.60 ³⁵	-	1.24 ± 0.36 ³¹ 3.73 ³⁶	9.02 ± 3.24 ³¹ 29.41 ³⁶	Yes ³⁷
Resveratrol	Yes (46%, 100 μM)	9.1 ³⁸	11.6 ³⁸	8.3 ³⁸	Yes ³⁹	Yes ³⁹	6.64 ⁴⁰ Yes ³⁹
Ellagic acid	Elevation (13%, 100 μM)	-	-	-	0.207 ⁴¹	-	Yes ³⁷

K_i values of OATP4C1 are expressed as mean ± S.E. Data for IC₅₀, K_i, or EC₅₀ values of the food ingredients are obtained from previous reports. Asterisk (*) indicates a K_i value instead of an IC₅₀

value. EC₅₀ value is expressed as mean \pm S.E. if the compound elevates the transporter mediated uptake. Yes, the food ingredients inhibited the transporter-mediated substrate uptake (inhibition degree, concentration of the flavonoid (if available)); No, no inhibition or elevation was observed; -, no data available; Elevation, elevation was observed.